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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/816,886

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Christian E. Gruber

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EXAMINER

TUNG, JOYCE

ART UNIT

PAPER NUMBER

1637

MAIL DATE

DELIVERY MODE

12/24/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/816,886	Applicant(s) GRUBER ET AL.	
	Examiner Joyce Tung	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 54-123 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 54-123 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The response filed 10/16/08 to the office action has been entered. Claims 54-123 are pending.

1. The rejection of claims 54-123 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn because of the amendment filed 10/16/08.
2. Claims 54-123 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Huo (5,922,535, issued Jul. 13, 1999) in view of Chenchik et al. (5,962,271, issued Oct. 5, 1999).

Huo includes the teaching of standard cDNA synthesis from mRNA (see column 5, lines 8-20). Huo also discloses the advantageous use of a biotinylated primer in cDNA synthesis to facilitate attachment of synthesized cDNA to solid supports (column 5, lines 21-27; column 7, lines 51-60; column 11, lines 31-37; column 12, lines 9-24). Huo also discloses the use a biotinylated primer comprising a rare restriction site (see column 13, lines 17-46).

Huo discloses several embodiments of the invention. One of the embodiments discloses that as depicted in Fig. 1, a biotinylated poly-T primer includes a rare restriction site at its 5' end, the primer is biotinylated either in the restriction recognition sequence or at the poly-T portion and after cleavage at least one biotinylated nucleotide is retained on 3' of the cleavage site (See column 13, lines 17-26). It is inherent in this teaching that the cleaved cDNA molecule is released and does not comprise a ligand portion of the primer-adapter nucleic acid molecule (See 17 of Fig. 1). Moreover, Huo also discloses that the cut site is filled in with biotinylated nucleotides (See column 13, lines 43-48). This teaching is inherent that the cleaved cDNA molecule does not comprise a ligand and the ligand is filled in after the cleavage.

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While Huo discloses the use of a biotinylated primer-adaptor comprising a rare restriction site, said primer-adaptor is used in a different manner than in the claimed methods; in Huo's heteroduplex cDNAs are produced which are cleaved at points of variation. In other words, Huo et al. covers steps (a)-(d) of claim 54, for example, but not steps (e).

Chenchik et al. disclose the use of cDNA synthesis primers comprising rare restriction enzyme cutting sites to facilitate cloning of full-length synthesized cDNAs into cloning vectors (see column 9, lines 17-25 and column 11, lines 40-45).

One of ordinary skill in the art would have been motivated to use a biotinylated adapter-primer comprising a rare restriction enzyme cutting site in conventional cDNA synthesis and subsequent cloning because Huo disclose the benefit of biotinylated cDNA synthesis primers in attaching cDNA to a solid support, and Chenchik et al. disclosed the benefit of cDNA synthesis primers having rare restriction sites in subsequent cloning of full-length cDNA into vectors. In other words, the skilled artisan considering the references as a whole would have combined the noted teachings to achieve the expected combined benefits of biotinylated primers of Huo and primers containing rare restriction sites (Chenchik et al.) in conventional cDNA synthesis. It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods.

The response argues that Huo does not use restriction enzymes to cleave the cDNA or RNA-DNA hybrid fragments from the solid support and Chenchik et al. do not teach binding of the cDNA to a hapten-cDNA molecule complex, nor release of cDNA from the complex using restriction enzymes. However, Huo disclose that a biotinylated poly T primer is used to promote synthesis of cDNA strands 7, 8 complementary to an mRNA population (see column 5, lines 21-

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24), PCR amplifies the cDNA strands 7 and 8 to produce double stranded DNA populations 9 and 10 (see column 6, lines 6-8 and 23-26) in which the double stranded DNA 9 has a mismatch and then the populations 9 and 10 are mixed (see column 6, lines 39-40) to produce a heteroduplex containing a mismatch (see column 6, lines 55-56), the heteroduplex is immobilized (see column 7, lines 51-54), the mismatch is cleaved by a mismatch-dependent cleavage reagent, for example S1 nuclease (see column 7, lines 62-67). The mismatched sequence is part of cDNA (see the teachings above). Huo also discloses the use of a biotinylated primer comprising a rare restriction site, the primer is used to make a cDNA copy of mRNA, the cDNA-mRNA duplex is converted into double-stranded DNA and subsequently the double stranded DNA is digested with NotI (see column 13, lines 17-46). Based upon the teachings of Huo, they cover the limitations of the instant claims except the limitation of inserting or ligating one or more of the cleaved cDNA molecules into one or more vectors. Nevertheless Chenchik et al. disclose the step of inserting or ligating one or more of the cleaved cDNA molecules into one or more vectors (see column 9, lines 17-25 and column 11, lines 40-45). Therefore, one of ordinary skill in the art would have been motivated to use a biotinylated adapter-primer comprising a rare restriction enzyme cutting site in conventional cDNA synthesis and subsequent cloning with the motivation as discussed in the rejection. Thus the rejection is maintained.

Summary

3. No claims are allowed.
4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

Joyce Tung
December 16, 2008